

## REMARKS

Applicants respectfully request reconsideration of the present application in view of the following commentary.

### **I. Status of the Claims**

Claim 73 was cancelled previously. Claims 1-72 are pending in the application. No amendments to the claims are introduced by this response.

### **II. Rejection of Claims under 35 U.S.C. § 102(b)**

Claims 1, 3-6, 9, 10, 12, 14-17, 26-29, 32-35, 38, 39, 41, 50, 52-55, 58, 59, 61 and 63-67 are rejected under 35 U.S.C. § 102(b) for alleged anticipation by U.S. Patent No. 6,184,220 to Türc̈k et al. ("Türc̈k"). Applicants respectfully traverse the rejection.

Türc̈k's composition is distinguished from the claimed compositions in several aspects: (1) As stated by the Examiner, Türc̈k fails to teach a surface stabilizer adsorbed on the surface of meloxicam particles; (2) Türc̈k fails to teach a composition comprising meloxicam particles having an effective average particle size of less than about 2000 nm; and (3) the  $T_{\max}$  of Applicants' claimed composition is shorter than that of Türc̈k's composition when comparing the same dosage strength and form.

#### **(A) Türc̈k fails to teach a surface stabilizer adsorbed on the surface of the meloxicam particles.**

Claim 1 requires at least one surface stabilizer adsorbed on the surface of the meloxicam particles. The Examiner explicitly acknowledges that, with respect to Claim 1, Türc̈k does not teach a surface stabilizer: "Türc̈k does not teach the claimed surface stabilizer" (Office Action, page 3, last full paragraph). For this reason alone, withdrawal of the anticipation rejection is warranted.

The Examiner's above-quoted statement that Türck fails to disclose a surface stabilizer is correct because Türck's composition requires a "three-dimensional solid structure" of silicon dioxide in which is carried the meloxicam (abstract and column 3, lines 45-52). Türck describes the three-dimensional silicon dioxide solid structure as a crosslinked, swollen and coherent strands of SiO<sub>2</sub> between which can be found fairly large cavities. The meloxicam is adsorbed almost exclusively onto and between the SiO<sub>2</sub> strands (column 3, lines 53-58). Türck's disclosure of a three-dimensional silicon dioxide solid structure is not a surface stabilizer and clearly fails to meet the claim limitation of "at least one surface stabilizer adsorbed on the surface of the meloxicam particles."

**(B) Türck fails to teach a composition comprising meloxicam particles having an effective average particle size of less than about 2000 nm.**

Türck discloses that "at least 90% of the particles are smaller than 50  $\mu\text{m}$ , preferably at least 50% of the particles are smaller than 10  $\mu\text{m}$ , and most preferably about 90% of the particles are smaller than 10  $\mu\text{m}$ " (column 4, lines 38-41). Claim 1 requires an effective average particle size of less than about 2000 nm. A D<sub>50</sub> of 10  $\mu\text{m}$  does not anticipate a D<sub>50</sub> (the claimed "effective average") of less than 2000 nm, i.e. 2  $\mu\text{m}$ . Likewise, a characterization of a distribution's D<sub>90</sub> does not provide information to one of ordinary skill in the art about the D<sub>50</sub> of that same distribution. For this additional reason, withdrawal of the anticipation rejection is warranted.

**(C) The T<sub>max</sub> of the claimed composition is shorter than that of Türck's composition when comparing the same dosage strength and form.**

Claim 1 requires a composition in "comparative pharmacokinetic testing with a non-nanoparticulate formulation [sic] to exhibit a shorter time to T<sub>max</sub> when compared to the time to T<sub>max</sub> of the non-nanoparticulate meloxicam formulation." Türck discloses that "the time for maximum plasma concentration on a single dose of meloxicam is t<sub>max</sub>=2 h (1.5-5 h; *suspension*)"

(column 9, line 67, through column 10, line 2). The Examiner contends that Türck's composition would have the same  $T_{\max}$  as Applicant's claimed composition because Türck teaches meloxicam having the same particle size as the Applicant's invention (see Office Action, page 3, first full paragraph). The contention is incorrect, and proven so by the McGurk Declaration submitted on April 3, 2008. If Türck's composition had the same particle size, Türck's suspension should have the same time to  $T_{\max}$  as reported in the McGurk Declaration. Such is not the case. In fact, the Applicant's nanoparticulate meloximan was reported to have a mean  $T_{\max}$  of 0.667 hours (see paragraph 8, Table 2), which is much shorter the mean  $T_{\max}$  (2 h) (and even the raw data, 1.5-5 h) of Türck's suspension.

Türck therefore does not teach the claimed limitation that the composition "in comparative pharmacokinetic testing with a non-nanoparticulate formulation of meloxicam having the same dosage strength and form, the composition exhibits a shorter time to  $T_{\max}$  when compared to the time to  $T_{\max}$  of the non-nanoparticulate meloxicam formulation." For this additional reason, the rejection cannot be maintained.

### **III. Rejection of Claims under 35 U.S.C. § 103(a)**

#### **A. Türck and Liversidge**

Claims 1-17, 26-42 and 50-67 are rejected under 35 U.S.C. §103(a) for alleged obviousness over Türck in view of PCT Publication No. WO 93/25190 by Liversidge et al. ("Liversidge"). Applicants respectfully traverse the rejection.

Notwithstanding the other deficiencies of the teachings of Türck, the Examiner acknowledges that "Türck does not teach the claimed surface stabilizer" (Office Action, page 3, last full paragraph), but relies on Liversidge to remedy this deficiency. The rejection requires one of ordinary skill in the art to remove the three-dimensional, solid matrix forming strands of  $\text{SiO}_2$  and replace it with the surface stabilizers of Liversidge.

As discussed above, Türk teaches that the SiO<sub>2</sub> forms a three-dimensional matrix of solid SiO<sub>2</sub> strands. Nothing in Liversidge teaches or suggests that its surface stabilizers are capable of forming such a structure. Despite the rejection citing to a general desirability of a less harmful (reduce gastric irritation) more stable (prevent agglomeration) composition, which applies to any pharmaceutical composition, the rejection fails to provide a specific reason why one of ordinary skill in the art would predictably expect that the surface stabilizers of Liversidge would perform the same as the three-dimensional, solid matrix forming strands of SiO<sub>2</sub>.

Accordingly, absent vague generalizations, the rejection lacks a rationale for one of ordinary skill in the art to make the simple substitution of one element for another. For at least these reasons, no *prima facie* case for obviousness has been made. In view of the foregoing, the rejection should be withdrawn.

**B. Türk and Desai or Courteille**

Claims 1-17, 26-42 and 50-67 are rejected under 35 U.S.C. §103(a) for alleged obviousness over Türk in view of PCT Publication No. WO 01/45706 by Desai et al. (“Desai”) or U.S. Patent No. 5,384,124 to Courteille et al. (“Courteille”). Applicants respectfully traverse the rejection.

The Examiner cited Desai and Courteille for their alleged teachings of the second particle population. Nevertheless, Desai and Courteille do not compensate for the deficiencies of Türk as discussed above. Therefore, withdrawal of the rejection is respectfully requested.

CONCLUSION

The present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested. The Examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by the credit card payment instructions in EFS-Web being incorrect or absent, resulting in a rejected or incorrect credit card transaction, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, Applicant hereby petitions for such extension under 37 C.F.R. §1.136 and authorizes payment of any such extensions fees to Deposit Account No. 19-0741.

Respectfully submitted,

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